Types of Immunity

I- Innate Immunity

- 1- Mechanical barriers (I,1)
  - S → Skin
  - M → Mucus
  - C → Cilia
- 2- Chemical barriers
  - A → Acids
  - L → Lysozymes → OPG
  - D → Defensins → TOXIC (CM)
- 3- Normal flora (I,2)
  - A → Attach.
  - N → Nutrients
  - B → Bacteriocins
- 4- Circulating effector prot.
  - Complement
  - Cytokines
  - Acute phase proteins
- 5- Cells (I,2)
  - Granulocytes: Neut., EOS., Mast, Bas.
  - Monocytes → MΦ (tissues)
  - Dendritic cells (tissues)
  - Lymphocytes (NK)
  - Functions
    - Phagocytosis
    - EC Killing
    - Inflammation

II- Adaptive Immunity

- CMI
  - Th ⊕
    - Th1
    - Th2
    - Effector
  - TC ⊕ → CTL
  - Treg → Downregulation
- HI
  - Bcells ⊕ → plasmacells (effector) → 5 classes of Abs: HAGED
- Memory cells
  - 2ry IR.

Components of Immunity

- Cells
- Protein molecules

Cells

I- Killer cells

- Phagocytic
  - MQ
  - Neutrophils
  - DCs
  - O_2 depend. (I, 9) — Free radicals (by oxidase) → ↑ph → suitable cond
  - Non O_2 dep. — Proteolytic enz.
- Direct EC Killing
  - NK
  - CTL
  - Eosinophils — Toxic basic protein
  - Perforins & granzymes

II- Non Killer

- Th1 (cytokines) — Il2 & IFNγ → ⊕ NK, MQ & TC (CMR)
- Th2 — Il4, 5, 6, 10, 13 → ⊕ B cells (HR)
- Basophils & Mastcells — Physiolog. mediators e.g. histamine → Inflam. in mucosa (VD)
- Plasmacells — Abs

III- Professional APCs → present Ag to Th

- MQ
- DCs
- B cells

Protein Molecules

- Surface
- Circulating

I- Surface Molecules

- Adhesion mol.
- CD mol.
- MHC mol.
- Receptors for Ag recognition

1- Adhesion Molecules: On immune & non immune cells

- Recruitment of leukocytes to sites of inf. (I, 7)
  - Leukocytes
    - Adhesion: L selectin
    - Rolling: Integrin
    - Rolling: P selectin
    - Sticking: Integrin Ligands (ICAM-1)
  - Endoth. cells
    - E selectin
    - P selectin
  - ↓ in leuk. adh. deficiency (II, 35)
  - IL8 induct
- Costimulation of T cells
  - ⊕ of Th & Tc by APCs
    - B7
    - ICAM-1 (APCs)
    - LFA-1 (Th & TC)
  - Recog. of target by CTL & its ⊕
    - B7
    - ICAM-1 (targets)
    - LFA-1 (CTLs)

2- MHC molecules: Biological importance (II, 17)

- MHC restriction (⊕ of T cells)
  - Class II
    - on APCs
    - ⊕ Th
  - Class I
    - On APCs
    - ⊕ TC
    - On VICs, cells è IC B & tumors to be recog. & killed by CTL
- Graft rejection
- Autoimmune ds
  - B27
    - Ankylosing spondylitis
  - DR4
    - Rheumatoid arthritis

3- CD molecules: Surface mol. with n°: 1,2,3 ....

- Each immune cell has specific CDs
  - Enumeration by flowcytometry to diagnose I D ds
    - CD14 — MQ, Neutrophils
    - CD3 — T cells
    - CD4 — Th
    - CD8 — TC
    - CD25 — Treg
    - CD19&20 — B cells
- Mediate important function
  - CD3 — ⊕ signal in T cell
  - CD4&CD8 — Coreceptor — Bind to MHC I & II → Stabilization of contact bet. APCs & T cell
  - CD28 — Reacts with B7 → Cost.
  - CD40&CD40L — Costimulation bet. T cells & APCs
  - CD95&CD95L — Fas & FasL → Apoptosis
  - CD59 — Regulation of Complement

4- Receptors for Ag recognition

- (I,8) PRR (pattern recog. recep) e.g toll-like R — Surface / endosome
  - MQ, Neut.
  - Recognize PAMP (pathog. ass. mol. pattern) on organisms
    - LPS
    - Tech. a
    - Viral DNA
- Specific Ag receptors
  - TCR/CD3 complex on T cells
  - BCR complex on B cells.

II. Circulating Molecules

- Cytokines
- Opsonins
- Abs
- Complement

1. Abs (Igs)

Structure (III 1,2)

- 2 Fab
  - Contains paratope or idiotype
  - Ag binding
- 1 Fc
  - Divides Abs into 5 classes (isotypes)
    - γ → G
    - μ → M
    - α → A
    - ε → E
    - δ → D
  - Biological functions of Abs

Forms (III 2,3,4)

- Membrane bound
  - Ag R on B cells: BCR
    - IgM & D on B plasma
    - IgG on Memory B
- Secreted by plasma cells
  - G: 1,2,3,4
  - M: 1,2
  - A: Binds to most in mucosa
  - E: inflammation
  - D

2. Functions of secreted Abs (III 10,11)

- Neutralization (by Fab) of bacteria, toxins & viruses
  - In blood: IgG
  - In mucosa: IgA
  - → Neutralizing Ab against toxoid vaccine protects from toxin
- Opsonization
  - G1 or G3 coat free org
  - Bind to Fc γ R (CD16) on MQ & Neutroph.
  - → IC killing
- ADCC
  - G1 or G3 coat VICs, tumor or Graft (not free org)
  - bind to Fc γ R on NK & MQ, Neut.
  - → EC killing
- complement activation
- IgE
  - Coats parasites
  - bind to Fc ε R on Eosinophils
  - → EC killing

2- Complement: Circulating inactive proteins

- **Source**
  - Liver
  - MQ
- **Forms** (III, 29)
  - C1→9
  - Other proteins
    - MBL, MASP-1&2
    - Factors B, D, Properdin
- **⊕ in cascade**
  - C2→5 enz. cleavage
    - a: Small → released
    - b: large → remain
  - C6→9 Covalent binding (no cleavage)
- **Pathways of activation**
  - **Lectin**: MBL binds polysacch. (G or M.) on bact. CW → ⊕ MASP-1&2
  - **Alternative**: C3b (by spontan. hydrolysis of C3) bind to Microbe
  - **Classical**: IgM or G3,1,2 bind Ag (Mic. or non Mic) → ⊕ C1

Innate Imm. — Adaptive (HI)

Functions of Complement (III, 32)

- **Membrane attack Complex (MAC)** C5b6789
  - Lysis (pores) of targets
    - Org: Bact., Fungi, Parasites, Env. V
    - VICs
    - Tumors & Graft cells
- **Inflammatory response**
  - **Chemotaxis**: C5a
  - **Anaphylaxis**: C3a, 4a, 5a → Bind to mast cells → histamine → D
- **C3b functions**
  - **Opsonization**: C3b coats org. → binds C3bR on MΦ & neutrophils
  - **↑ Ab prod.**: C3b binds to C3dR on activated B cells
  - **Removal of harmful ICs**: ICs → C3b binds IC → binds to C3bR on phagocytes

3- Cytokines:

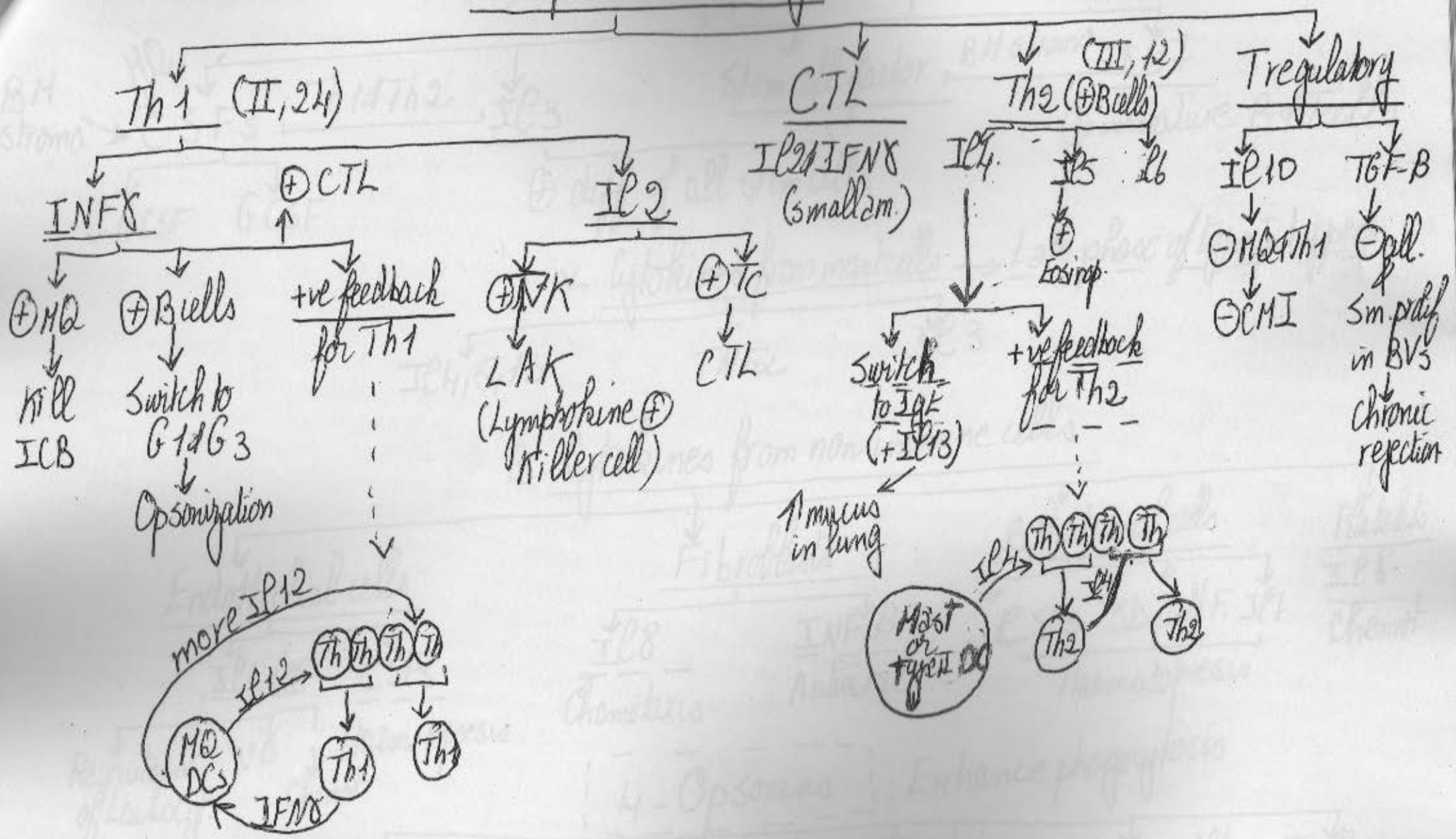
From immune from immune cells ← 3- Cytokines: → In response to infections ---> Cellular commun. (rapid due to low Hs) → Binds specific R.

A- Cytokines from immune cells

i- Innate Immunity

- MΦ & DCs
  - Inflammatory (I, 5)
    - Acute inflam. response (AIR)
      - TNFα, Il 1 & 6
      - i. ↑ exp. of Ad. M on End. & Leuk. → Recruitment & ⊕
      - ii- End. Cs: VD & ↑ coagul. Fs & ⊖ anticoag. Fs
      - iii- ⊕ liver → acute phase proteins
      - iv- Fever } by TNF & Il 1
      - v- Muscle wasting → Cachexia
    - Chemokines
      - Il 8
      - → Chemotaxis
    - Il 12
      - → ⊕ NK
      - → Th 1 form.
- CSFs: hematopoesis
  - Antiviral
    - IFNα
      - → ⊖ viral repl. (adj. cells)
      - → ⊕ NK
  - Inhib.
    - Il 10
- NK cells
  - IFNγ
    - → ⊕ MΦ
    - → ⊕ Th 1 & CTL

iii. Adaptive Immunity



(III, 15) iii- Haematopoesis : ⊕ of immature WBCs in BM

- BM stroma → CSFs (HQ) — Th1 & Th2
  - GMCSF
  - GCSF
- IL3 — ⊕ diff. of all stem cells
- Stemcell factor — BM stroma
- IL7 — ⊕ immature B & T cells

iv- Cytokines from mastcells → Late phase of type I hypers.

- IL4, 5, 13
- TNFα
- IL3

B- Cytokines from non immune cells

- Endothelial cells
  - IL1, 6, 8
    - Recruitment of Leukocyt.
    - VD
    - Chemot.
  - CSFs — Haematopoesis
- Fibroblasts
  - IL8 — Chemotaxis
  - INF β — Antiviral
- BM stromal cells
  - CSFs
  - Stemcell F.
  - IL7
  - Haematopoesis
- Platelets
  - IL8 — Chemot.

4- Opsonins : Enhance phagocytosis

- (I, 3) MBL & C reactive proteins (acute phase proteins)
  - From liver
  - under effect of TNFα, IL1 & IL6
  - Also ⊕ Compl.
- C3b
  - Alt.
  - Lectin
  - Classical
- IgG

Types of Organisms

IC org

- Few bact. e.g TB
- Viruses
- Fungi

Def. in neutroph → Recrr. fung. inf

- Live inside MQ → MQ must be ⊕ by IFNγ from Th1
- Live inside cells → Infected cells must be killed by NK, CTL ⊕ by IL2

(II, 36) Digeorge synd ← Deficiency in CMI → Recurrent IC infections

No 3rd & 4th pharyngeal pouch

ECB & their toxins (Acute pyogenic)

Affect. by Ab

- Neutraliz
- Opsonization by MQ & neut.
- Complem. ⊕

Def. in B cells, phagoytes & Compl. → Recurrent pyogenic inf.

X linked agammaglobulinemia (III, 19)

Failure of BM to generate mature B cells

Parasites

- EC → ADCC by IgE & eosinophils
- IC
  - Inf. cells are Killed by CTLs
  - Repl. in MQ

Relation between Innate & Adaptive Immunity

I- Innate cells ⊕ Adaptive cells by

- **Ag presentation: APCs**
  - MQ & DCs process protein Ags in tissues (After killing org. IC)
  - ↓ Present it with MHC
    - Class II → ⊕ Th
    - Class I → ⊕ TC
    - in 2ry L.O
- **Cytokines**
  - IL1 (from MQ & DCs)
    - ⊕ Th & TC (costimul.)
    - ⊕ Bells
  - IL12 → Th1 formation
  - IFNγ (from NK) → ⊕ Th1 & CTL

II- Adaptive cells ⊕ Innate cells

- **INFγ** (from Th1 & CTL) → ⊕ MQ to kill phagocytosed IC org
- **IL2** → ⊕ NK → LAK
- **IgG1 & 3** (from Bells)
  - MQ & Neut. → Opsonization
  - NK & MQ → ADCC
- **IgE**
  - Eosinophils → ADCC of parasites

Inflammation

- VD ←
- → Recruitment of leuk. to sites of inf.
- Inflamm. cytokines: TNFα, Il1, 6, 8
- Inflam. cells in Mucosa: Eosinophils, Basophils, Mastcells.

Phagocytosis (II, 7)

I- Resident MΦ & DCs recognize Microbes
- → PRR ← PAMP
- → C3bR ← C3b coats org (Lectin, Alt.)

↓

II- Release of proinflam. cytokines (End. Cs: Il1, 6, 8)

- Recruitment of Neutroph (TNFα, Il1, 4, 6): A → Adhesion, R → Rolling, S → Sticking, S → Spread
- VD → Extravasation (squeezing)
  - Also by histamine from mastcells
  - C3a & C5a ← Also by
- Chemotaxis: by Il8
  - Assessed by Modif. Boyden Chamber assay (II, 35)

↑↑

- Super Ag → Septic shock (II, 29)
  - Systemic VD → shock
  - anticog. F → DIC
  - Myocar. contract. → HF
- Type IV Hyp. (II, 30)
  - Tuberculin test
  - Granuloma
- Tumor (IV, 2) — TNFα
  - Apoptosis
  - Thrombosis of BVs.

↓↓

- Fungi (II, 28)
  - prod. from MΦ
  - evasion of IR
- Anti TNFα (Monoc. Abs)
  - tt of Rheum. arthritis (IV, 13)

↑ Prevent GR (graft rejection)

- CCs (IV, 11) — corticosteroids

III - Uptake (I,8)

Attachment → Phagosome + lysosome → phagolysosome

IV - IC Killing (I,9)

A- Mechanisms : Oxidative & non oxidative

B - Resistance to killing

- ICB & parasites (II,26)
  - ⊕ MQ by IFNγ from Th1
- Evasion of IR by ICB
  - Disruption of phagosome
    - Escape into cytoplasm
    - e.g Listeria
  - ⊖ of phagolysome
    - e.g TB
    - Legionella
  - Inactivation of ROM
    - e.g. leprae

C - Defective Killing (II,35)

- Defect in Lysosome : Chediak Higashi
  - No fusion with phagosome → Giant lysosomes
- ↓ oxidase → ↓ production of ROS
  - Chronic granulomatous ds → diagnosed by NBT
    - ↓ remain yellow

V - EC Killing (without ingestion)

- Parasites (III,18)
- Tumor (IV,2,4)
  - (except if killed by CTL & NK)
  - BCG is given in tumor
    - ⊕ MQ
- Graft cells (IV,7)
  - Chronic delayed hypersens.

Outcome of phagocytosis (I, 9)

- **Neutrophils**: Destroy org. completely
- **MQ & Dendritic**: APCs
  - Process Ag → Present it to T cells

Sequence of events in Imunity

BM synthesizes & releases

- **Monocytes** → MQ in tissues
- **DCs** → tissues
- **Mature NK** → blood / tissue
- **Mature B cell**: Express BCR recogn. foreign Ag (after -ve selec.)
- **Immature Thymocytes** → **Thymus** → +ve sel. / -ve sel.
  - Express TCR recog. Foreign Ag + self M.

MQ in tissues / tissues:
- Induce Inflamm (together with compl. & mastcells)
- Process Ag

2ry L.O: Spleen, LNs & MALT

Mature naive B cells — Mature naive T

in T DAgs ← presente MHC II to Th

presentation with MHC I & II to TC & TH

Important Ags

- MHC
  - Self → Ag presentation
  - Foreign → Graft reject.
- Tumor Ags
- Heterophil Ags → AID
- Hapten → Drug hypersensit.
- Sequestered Ags
  - AID
  - Im escape
  - No GR
- Adjuvants

Epitope (III,4)

Smallest biach. unit of Ag that ⊕ Ag R on B&T binds to paratope of secreted Ab

Types: 1 Ag may have
- Several different epitopes e.g protein Ag ⊕ different B cells
- Several identical epitopes e.g CHO (polysacch.) Ag ⊕ 1 B cell

Tumor Ags (IV,4)

→ weak immunogen → tumor evade IR → Grow

Escape (evasion) (IV,3)
- Hidden
  - Glycocalyx
  - Privileged sites
- Masked
- Lost
  - Non cytotoxic Abs
  - High mutation rate

Tumor specific Ag
- Altered self proteins
- Products of mutated
  - Protooncogene
  - Tm. supp. gene
- Products of oncogenic V

Tumor non specific Ags: Oncofetal Ags
- Expressed in Fetus
- Silenced in adult
- Reexpressed in tumors

e.g α fetoprotein → HCC
Carcinoembry. Ag → cancer colon

Markers in tumor diagnosis

Maturation of T cells : Thymus

1- TCR / CD3 complex (II, 18)

TCR
- V of α and β
- Diversity

V of α and β → Recognize self MHC ← +ve selection (cortex)

Recognize self MHC → Need APCs

Foreign Ag (pept) (complementary to it) ← -ve selection → Central tolerance (medulla)

-ve selection → doesn't occur for sequestered Ags

CD3 : ⊕ signal

2- CD4 or CD8

CD4 → Th (65%) → Interacts with MHC II on APCs

CD8 → TC (35%) → Interacts with MHC I on APCs / Infected cells or tumor cells

Released to 2ry L.O : spleen, LNs, MALT

Maturation of B cells : BM

BCR complex (III, 3)

BCR
- V of H & L chains of memb. bound IgM & IgD → Monomeric
- Diversity
- Recognize foreign Ag
  - Free (without MHC)
  - All forms
  - -ve selection → Central tolerance

Igα and Igβ : ⊕ signal

Several BCR must be occupied simultaneously (T indep. Ag = polysacch.) or no ⊕ unless activated by Th (T dep. Ag = protein)

↓

B cell acts as APCs

Released in 2ry L.O : spleen, LNs & GALT

MHC

I- Classes & Structures : (II, 15)

II - Source of expressed Ag (Role in Ag presentation) : 2 pathways (II, 16)

A - MHC II : for ingested Ags

- Only by APCs
  - ⊕ Th in LNs
- Allorg
  - EC
    - only pathway
  - IC
- Tumor Ag
- ↑↑ by IFNγ (II, 24)
- ↓↓ by IL10 from Treg. (II, 25)

B - MHC I : for newly synthesized Ags

- ↑ by IFNγ
- ↓ by IL10
- By APCs
  - ⊕ of mature naive TC in LNs
- By → to be recognized & killed by CTL in tissues
  - VIC (II, 23)
    - ↑↑ by IFNα
    - By Adenov.
      - evade IR
  - Tumor cells (IV 2,3)
    - ↓↓ by some tumors
      - Escape
    - ↑↑ by IFNγ & TNFα
  - Cells è ICB (II, 23)

Killed by NK cells (released from normal state of ⊖ caused by KIR : Killing ⊖ receptors)

T cell activation (II 20,21)

I- Recognition of Ag : 1st signal

- TCR
  - Ag
  - MHC
- CD4 (Th) → MHC II
- CD8 → MHC I
- (stabiliz.)
- CD3 → ⊕ signal
  - Anti CD3 (Mc Ab) → Kill T cells by complement → Prevent GR

(II, 28) Super Ags < binds MHC II outside peptide bind. groove; Binds to specific β

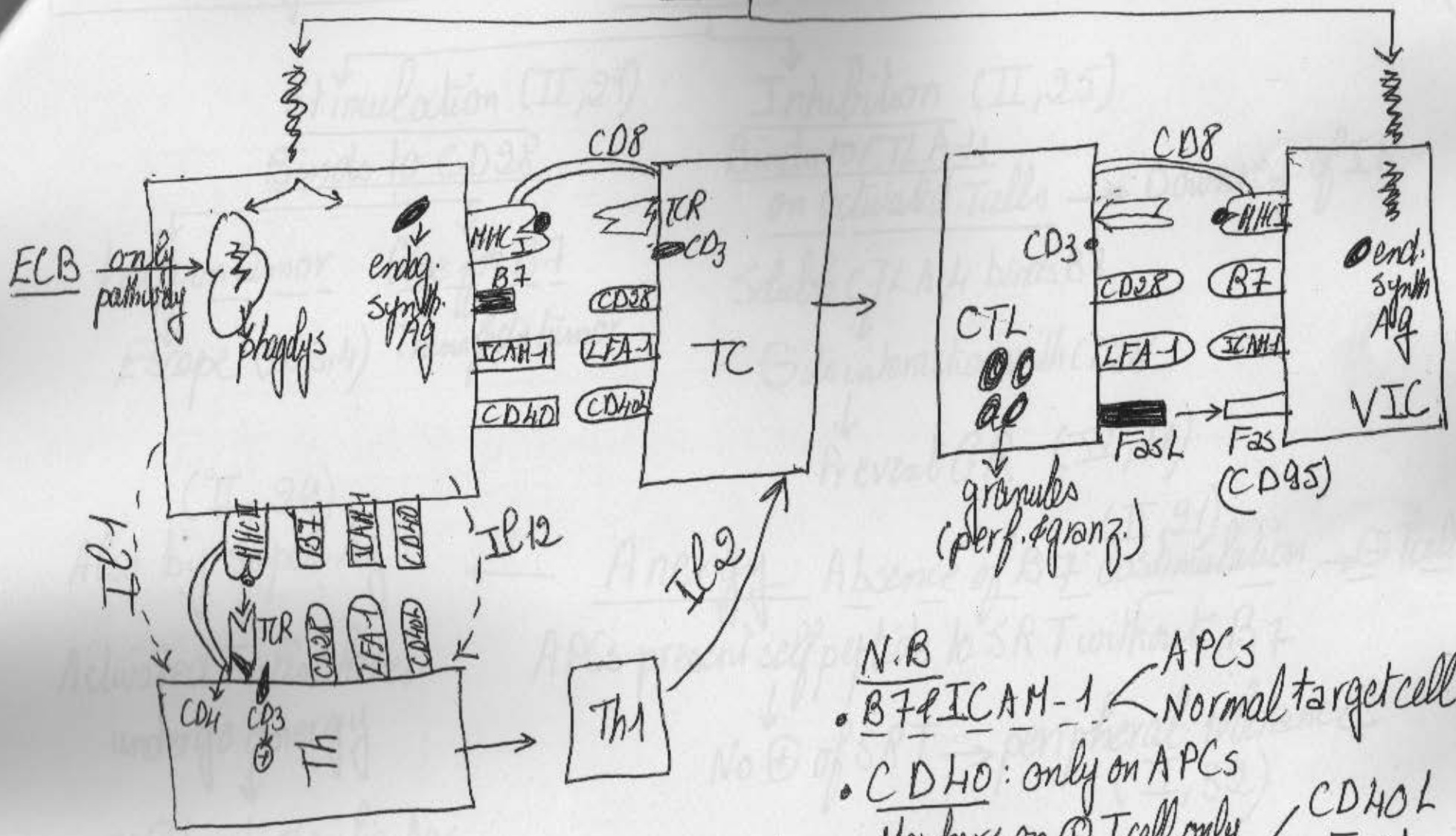
II - Costimulatory mol. needed for activation

- 3 surf. mol
  - APC
    - B7 ---> CD28
    - ICAM-1 ---> LFA-1
    - CD40 ---> CD40L (partially activated)
  - T cell (Th or TC)
  - ↑ by INFγ
  - ↓ by Il10
- 1 cytokine
  - Il1 from MΦ, BC → ⊕ Th
  - Il2 (from Th1) → ⊕ TC
    - Injection → non sp. ⊕ in tumor
    - Gene of Il2 → Transfect tumor
    - Adoptive therapy → TC or NK from pt. blood or tumor → Il2 in vitro → Back to pt
    - (Immunotherapy for tm) IV, 4

(IV, 11) Il 2 inhibitors → prevent graft rejection

- ↓ production
  - Cyclosporine
  - FK506
- ⊖ Recept. on TC → ⊖ signaling
  - Rapamycin
- ⊖ Binding to Rec
  - Anti Il2 R

2 viruses or ICB or tumors (II. 20,21)



N.B

- B7 & ICAM-1 < APCs, Normal target cells
- CD40: only on APCs
- Markers on ⊕ T cell only < CD40L, FasL, CTLA-4

Costimulatory mol.

A – B7

Stimulation (II, 29)

Binds to CD28

- ↓exp. on tumor → Escape (IV 3,4)
- Gene for B7 → Transfects tumor

Inhibition (II, 25)

Binds to CTLA-4 on activated Tells → Downreg. of IR

Soluble CTLA-4 binds B7
↓
⊖ its interaction with CD28
↓
Prevent GR (IV, 11)

Anergy: Absence of B7 costimulation (II, 29) → ⊖ Tcell (arrest)

APCs present self peptide to SRT without B7
↓
No ⊕ of SRT → peripheral tolerance (II, 32)

← Also by super Ag (II, 29)
↓
Activated Tcells clones undergo anergy
↓
no ⊕ by its specific Ags

B_CD40-CD40L

1- Essential for ⊕ of T cells

- Anergy of SRT (II, 32)
  - APCs present self peptide cout CD40
- Mutation in gene coding for CD40L in T cell (III, 19)
  - Hyper IgM synd. (CMI is also defective)

2- Essential for ⊕ of B cell & Class Switch

- T cell depend. Ag: proteins (III 5,6)
  - Undergo Switch
    - Change in CH. chain but maintain VH&VL
  - CD40L → CD40
  - INFγ → G1&3
  - IL4&13 → E
  - ↓
  - (II, 32) Helplessness (peripheral tolerance)
    - SRB recognizing self Ag don't receive help from inhibited SR T cells
    - ↓
    - SRB die by apoptosis
- T cell independent Ag: polysach (III, 7)
  - No Costim → No switch or memory
    - only IgM
  - ↓
  - Vaccines containing polys. capsules are weak Igen
    - Conjugated with protein
    - Anticidiotypic vaccines.

CTLs

Importance: Main effector in
- Tumor
  - TILs
- GR
- VIC
  - Similar to those by MAC

Mechanisms of Killing: Apoptosis (II, 22)
- Perforin pathway
  - pores
  - Granzymes enter
- FasL–Fas path. (II, 23)
  - (on CTL) (on target)

Assessed by Cytotoxic T lymph. assay (II, 37)

Mix CD8 with target cell containing radioactive Na chromate

Assess radioactivity in supernatent

Differences from NK
- Target recog. + Killing + Thymus maturation
- Small
- Memory cells

Fas-FasL (CD95-CD95L)
- Killing by CTL (II, 22)
- Programmed death in leukoytes (IV, 3) (Tumor evasion)
  - Tumors express FasL
  - Kill Leukoytes exp. Fas
- Tolerance → prevent AID
  - Central (II, 32)
    - -ve selection in Thymus
  - Peripheral: in LNs
    - Activation induced cell death
    - SRT exp. Fas & FasL → Mutual apopt.
    - Genetic defect → AID (II, 33)

Type IV : CM or delayed (II.30,31)

Th1 (main)

Tuberculin skin test

1st exp. to T.B (inf. or BCG vaccine)

↓

Sensitized & Mem. Th1

↓

⊕ by ID inj. of PPD (2nd exp)

DCs carry Ag to L.Ns ↓ 48 hrs → ⊕ Sens. Th1

Erythema & Induration

Erythema ← I.D ← ⊕MQ ← INFγ ; Erythema ← ~~Inf.~~ ← TNF

Induration ← MQ (Mostly) ; Induration ← Th1

CTLs (main)

- Contact dermat.
  - Topical hapten (Ren., Cosm., heavy met)
  - binds to S.P. ↓ Ag pred. by Lang. cells
  - ⊕ lymph. & MQ (mononucl. infiltrate)
  - ↓ (12-15 hrs)
  - Eczema + edema in Epid.
  - ↓ Diagnosis
  - Patch test (Apply Ag for 24-48 hrs)
- IDDM
  - CTLs to panc. Ags
- Transpl.
  - Ch. Rej.
  - Acute Rej

Th1 (main): Granuloma

Chronic inf. in MQ with IC org → T.B / → Leprosy

⊕ of Th1 → ↑ cytokines (IFNγ)

⊕ → MQ → Epithelioid → Giant cells

→ Fibrosis → Hardening

Wall off site of persist. inf.

2 Skin tests with different pathogenesis

Pathological effects of CMI

- Super Ag
  - Th1 & MQ
- Type IV : Delayed hyper.

Down regulation of IR

CTLA-4 ← Down regulation of IR → Treg

Ag sp
↑
TCR CD4 CD25 specific
CD3

Treg (II,25)

→ ⊖ SRT that escaped (II,32)
-ve selection (periph. tolerance)
↓
↓ Treg. with Age
↓
AID (II,33)

Down reg. immunity by ←
IL10 & TGF-β (inhibitory cyt.)
↓ produced by
- Tumors → Evasion (IV,3)
- Epstein-Barr V (similar to IL10) → Evasion (II,27)
- Parasites → Evasion (III,18)

Early ⊕ by
- Tumors (IV,3)
- Fungi (to prod. IL10) (II,28)
- parasites

Evasion

IL10
Also by MQ & Th2
⊖ → MQ
⊖ → Th1
⊕ → B cell → Ab prod.

MQ
- ↓ IL12 → ↓ Th1
- ↓ MHC I, II & Costimulators → ↓ Ag present.

Th1
- ↓ IFN γ

TGF-β (IV,7)
⊖ → B cells
⊖ → MQ & Th
↑ due to repeated acute rej.
↓
Thickening of arterial wall
↓
Luminal occlusion & graft fibrosis
↓
chronic rejection (after ms)

Complementary notes on Abs

Structure & related Functions

(25) Selective IgA def.
Recurrent GIT & RT inf.
(III, 19)

Delayed onset of Prod. + ↓ transm. from mother
Transient Hypogammaglobul. in infancy
(III, 18)

IgG (III, 9)

Monomer → Lowest MW
- Diffuses EV
- Crosses placenta (except G2)

IgM

Pentamer → Highest MW
- IV
- Doesn't cross placenta
  - Intrauterine inf
- Most powerful
  - Agglutinat.
  - Comp. Act.

sIgA

- Dimer
- Secretory piece only in sIgA
- A1 protease is prod. by bact
  - A2 is more imp.

Humoral Immunity against tumors

(IV 2,34)

3 effector mech.

- ADCC — NK — IgG
- MAC — IgM — Comp. (+)
- Tumor

- CTL, NK — Tumor
- opsonization — MΦ

Non cytotoxic Abs

Mask Tumor Ags
Evasion

- Tm — CTL — Masked Ag from CTL
- Shedding
  - Tm — loses Ag
  - Tm → NK/MΦ — FcR is blocked — No ADCC

Passive immunotherapy (Specif.)

Mc Ab against Tm Ags

- Free
  - Tm — Lysed by Comp (+), ADCC
- Magic bullet
  - drug → Radioisotope
  - Tm — Lysis
  - Normal cells aren't affected

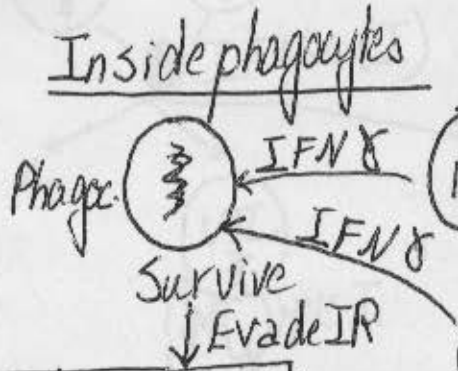
Comparison between T helper 1 & T helper 2 cells

	Th1 cells	Th2 cells
1-Formation	By **IL12** secreted from **MQ & DCs**	By ***IL4*** secreted from ***mast cells***
2-Main role	Immunity against **IC** bacteria ,**viruses,fungi** & **tumor cells**	Immunity against ***EC*** bacteria &***their toxins + parasites***
3-Cytokines production	**i.IL2, IFNγ and TNF α & β**	***i.IL 4,13,5,6 & 10***
	ii.IL3 & GM-CSFs	
4-Cytokines functions	**i. ⊕ MQ** to kill IC org.(IFNγ) **ii.↑ cytotoxicity of Tc & NK cells** (IL2) **iii.↑ production of opsonins:IgG1&G3** (IFNγ) Coat org. ⬇ Bind to Fcγ R on phagocytes ⬇ Opsonization	***i.⊕ eosinophils*** to kill helminthes (IL5) **ii.⊕B cells** ↑Ab production & isotype switch
5-Harmful effects	**Delayed hypersensitivity** (type IV)	***Anaphylaxis & atopy*** *(type I)*
6- +ve feed back & cross regulation	Cytokines produced by **each subset**	
	Positively regulate the subset producing it	***Negatively regulate*** the other subset
	IFNγ from Th1 ⬇ ⊕ MQ & DCs ⬇ More IL12 production ⬇ **More Th1 &⊖generation of Th2**	***IL4,10 & 13 from Th2*** ⊖MQ ⬇ ***⊖ generation of Th1 &*** ***IL4 ⊕ generation of Th2***

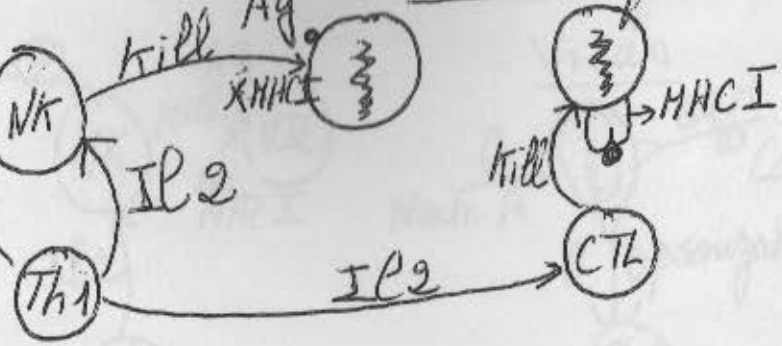
Immunity against Microbes

(II, 26) I - ICB : CMI

Inside phagocytes

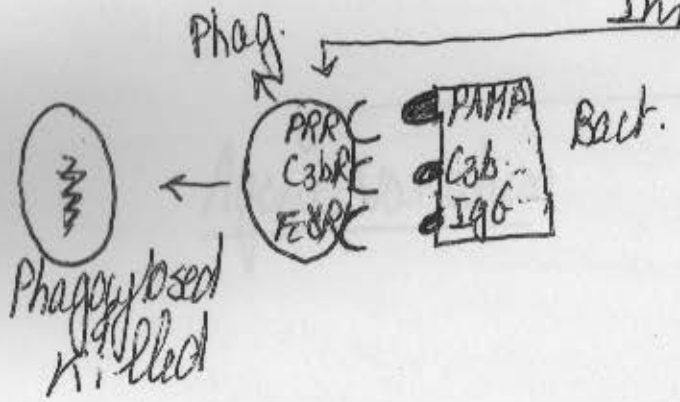


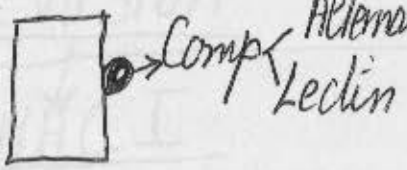
Inside Infected cells



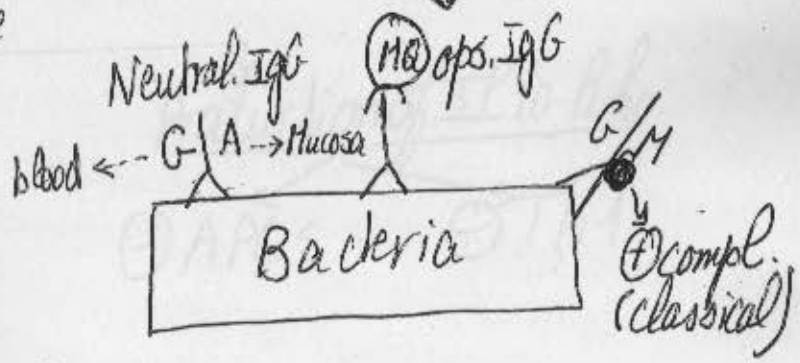
II - ECB : HI (III, 16)

Innate





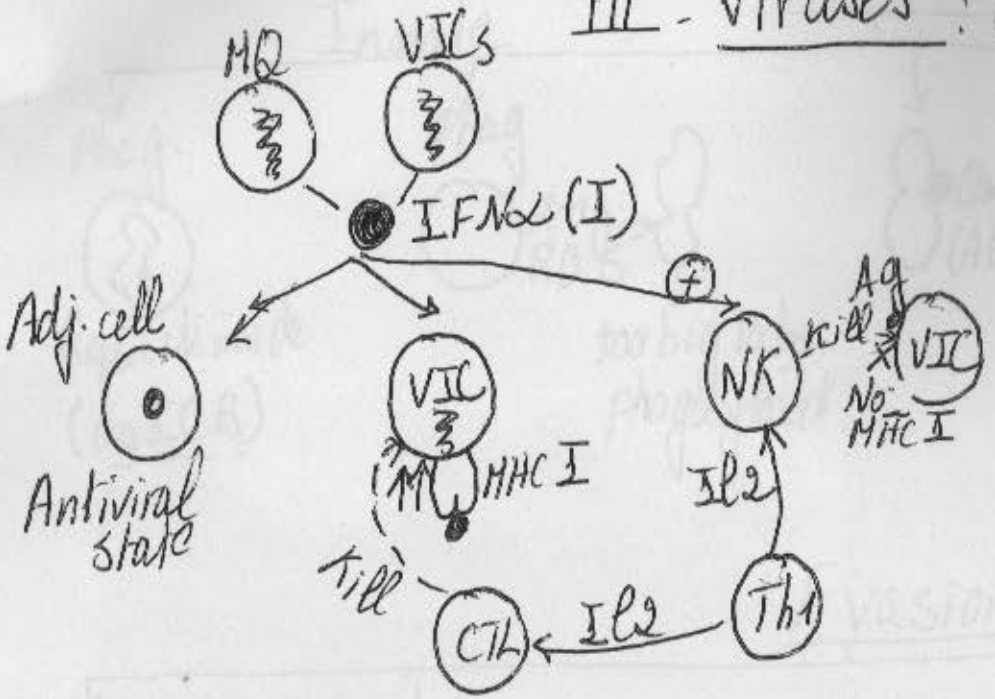
Humoral

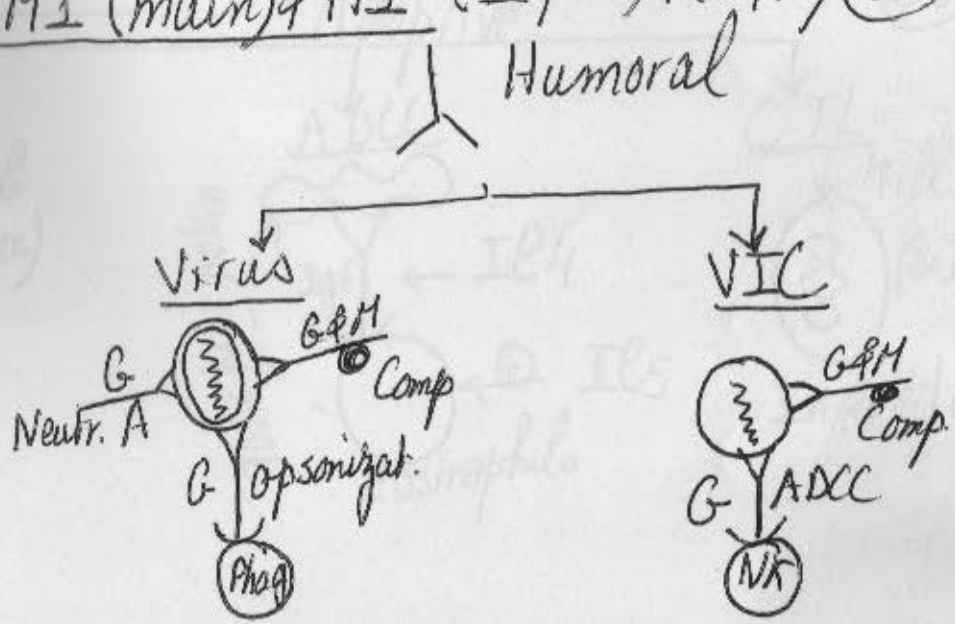


Evasion

- Agenic variation
- Sialic acid in capsule
  - ⊖C3b dep. in alternative pathway

III - Viruses : CMI (main) & HI (II, 27) + (III, 17) (98)





Evasion

- Agenic variation
- ↓MHC I
  - ↓Ag Pres.
  - ↓Recog. by CTL
- Production of Il10-like
  - ⊖APCs
  - ⊖Th1

IV - Parasites (III, 18)

Innate

- Phag. → Replicate inside (as ICB)
- Phag → enz. ROS → too big to be phagocytosed
- Compl. (Alter.)

Adaptive

- ADCC → Toxic basic protein; IgE; ← Il4; ⊕ Il5; Eosinophils
- CTL → kill (as ICB) Infected cells

Evasion

- Agenic Variation
- IS
  - ⊖ cytokines e.g Il10
  - ⊕ Treg
- Thick tegument
- Cysts

V - Fungi : CMI (mainly) & HI (II, 28)

- Neut. & MΦ
  - Neut. def. due to BM supp. → ↑ Fungal inf
- CMI
  - Th & TC
  - Evasion: ⊖ MΦ
    - ↑ Il10 from Treg → ⊖ MΦ
    - ↓ TNFα & Il12 from MΦ
- HI
  - ADCC